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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,149	10/19/2001	R. Preston Mason	2189 P01 US CIP	2552

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EXAMINER	
BAHAR, MOJDEH	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,149	MASON, R. PRESTON	
	Examiner	Art Unit	
	Mojdeh Bahar	1617	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *29-56 and 60-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a CIP of 09/556,930, now abandoned.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-28 and 57-59, drawn to a pharmaceutical composition comprising amlodipine and an atorvastatin metabolite, classified in class 514, subclasses 423 and 356.

II. Claims 29-56 and 60-62, drawn to a method of treating heart diseases employing a pharmaceutical composition comprising amlodipine and an atorvastatin metabolite , classified in class 514, subclass 423 and 356.

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case heart diseases, e.g., hypertension can be treated with ACE inhibitors or beta-blockers.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Specie Election

Claims 29-56 and 60-62 are generic to a plurality of disclosed patentably distinct species comprising, heart disorder or conditions. Applicant is required under 35 U.S.C. 121 to elect a

single disclosed species, even though this requirement is traversed. The treatment of each heart disorder or condition represents a separate field of medical technology having a separate field of search. The search for treatment of all heart disorder or conditions is therefore an undue burden on the office. Note that the search is not limited to patent files.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that in order for the reply to this requirement to be complete it must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

During a telephone conversation with Mr. Cohen on 03/14/2002 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-28 and 57-59. Affirmation of this election must be made by applicant in replying to this Office action. Claims 29-56 and 60-62 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

Claims 4-21 and 25-28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent

form, or rewrite the claim(s) in independent form. Note that the recitation of intended use does not further limit a claim drawn to a composition.

Claim 1 is objected to because of the following informalities: The employment of parenthetical expression "(ATM)" is informal. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-28 and 57-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The expression "formulation agents" in claims 1, 22 and 57 renders the claims indefinite. What is a "formulation agent"? Is it a pharmaceutically active agent? Is it an excipient? Is it a dosage form?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-28 and 57-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davison et al. (USPN 4,879,303) and Bjorge et al. (USPN 5,385,929) in view of Jukema et al. and Merck Index.

Davison et al. (USPN 4,879,303) teaches a pharmaceutical composition comprising amlodipine besylate useful in treating ischemic heart disease, angina or hypertension, see claim 1 and abstract in particular.

Bjorge et al. (USPN 5,385,929) teaches a pharmaceutical composition comprising ortho, meta, para hydoxylated metabolites of atorvastatin and a pharmaceutical carrier useful in inhibiting cholesterol synthesis, treating hypercholesterolemia, atherosclerosis, see claims 12, 18 and abstract.

Davison et al. (USPN 4,879,303) and Bjorge et al. (USPN 5,385,929) taken together do not teach a pharmaceutical composition comprising amlodipine besylate and a hydroxylated metabolite of atorvastatin.

Jukema et al. teaches that the addition of a calcium channel blocker to HMG CoA Reductase inhibitor therapy (pravastatin) acts synergistically in retarding the progression of coronary atherosclerosis, see abstract.

The Merck Index Therapeutic Category and Biological Activity Index lists atorvastatin as a HMG-CoA Reductase Inhibitor, belonging to the same therapeutic group as Pravastatin, see THER-10. Further, The Merck Index Therapeutic Category and Biological Activity Index lists amlodipine as well as other calcium channel blockers as antihypertensive agents.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ amlodipine besylate with atorvastatin metabolites in a pharmaceutical composition.

One of ordinary skill in the art would have been motivated to employ amlodipine besylate with atorvastatin metabolites in a pharmaceutical composition useful in a method of treating cardiovascular diseases such as hypertension, hyperlipidemia and atherosclerosis because atorvastatin is a known HMG Co-A reductase inhibitor and is therefore expected to have therapeutic effects similar to pravastatin. Similarly, amlodipine is a known calcium channel blocker. One of ordinary skill in the art would have been motivated to employ the known antihyperlipidemic metabolites of HMG CoA Reductase inhibitor atorvastatin for example, with the known calcium channel blocker, amolodipine besylate in a single pharmaceutical composition useful in treating heart disease since the combinations of agents known to be useful individually for the same purpose into a single combination useful for the very same purpose is prima facie obvious. *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069 (CCPA, 1980). All actives recited in the claims are known to be useful in the treatment of heart disease. Therefore, combining all of these active agents in a composition or method useful in treating osteoporosis is *prima facie* obvious. Moreover, the skilled artisan would combine the two agents because the addition of calcium channel blockers to HMG CoA reductase inhibitory therapy is known to have a synergistic effect in treating atherosclerosis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The

examiner can normally be reached on (703) 305-1007 from Monday, Tuesday, Thursday and Friday from 8:30 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
March 20, 2002

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
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